

Hypertension in elderly patients

Recommended systolic targets are not evidence based

Michael Allen MD MSc Kim Kelly Isobel Fleming ACPR

Hypertension, which accounts for approximately 7% of all visits, second only to colds and sinusitis,¹ is a condition that family physicians manage routinely, so much so that our beliefs and practices can become ingrained and second nature. We might not realize the uncertainty behind some practices in our management of hypertension, especially in elderly patients. The purpose of this commentary is to inform family physicians of the uncertainty in the evidence for a systolic blood pressure (SBP) of lower than 140 mm Hg as a therapeutic target in elderly (65 years or older) and very elderly (80 years or older) patients. We are concentrating on SBP rather than diastolic blood pressure (DBP) because current thinking considers SBP more relevant for determining cardiovascular risk in patients with hypertension, particularly in those older than 50 years of age.²⁻⁴

In elderly and very elderly patients, there is good evidence that treating hypertension leads to clinical benefits. A 2009 Cochrane review that included 15 studies and approximately 24 000 subjects found that treatment improved rates of cardiovascular and cerebrovascular morbidity and mortality.⁵ While the Cochrane review confirms there is benefit in treating hypertension in this population, there is uncertainty about the optimal SBP that should be achieved and maintained. Evidence about the optimal SBP target comes from 2 main types of trial.

- Drug treatment trials randomly assign patients to a specified treatment. The comparators can be one drug or regimen versus another drug or regimen or versus placebo. Patients randomly assigned to the different comparators might have a reduction in adverse clinical outcomes and achieve different SBPs that are used to make recommendations. However, particularly in placebo-controlled trials, it can be hard to determine if the benefit in outcome comes only from lower SBP or from effects of the drugs independent of blood pressure (BP) lowering (eg, angiotensin-converting enzyme inhibitors and calcium channel blockers can affect cardiac and stroke outcomes, respectively).⁶
- Treat-to-target trials randomly assign patients to 2 different SBP targets, but the 2 groups are treated with the same or similar drugs. Therefore, a difference in outcomes can be attributed to the different SBP targets.

The preferred type of study to address the optimal SBP target is a treat-to-target trial. However, most conducted

studies have been treatment trials. The Canadian Hypertension Education Program guideline recommends an SBP treatment target of lower than 140 mm Hg regardless of age. This is a grade C recommendation, indicating it is based on low-quality trials, unvalidated surrogate outcomes, or results from non-randomized observational studies. The guideline does not cite the studies on which the recommendation is based.⁷

Drug treatment trial outcomes

A re-appraisal of the 2007 European Society of Hypertension guideline reviewed the achieved SBPs in the comparator arms of 9 important drug treatment trials in elderly patients.⁸ All but 2 achieved SBPs lower than 160 mm Hg in the active treatment groups but none achieved SBPs lower than 140 mm Hg. However, all showed benefit in clinical outcomes. Thus, evidence from these treatment trials supports a potential benefit from an SBP target of lower than 160 mm Hg but does not support an SBP target of lower than 140 mm Hg in elderly patients. A 2011 consensus document prepared by the American College of Cardiology Foundation and the American Heart Association (ACCF-AHA) states that in elderly patients, the generally recommended goal of BP lower than 140/90 mm Hg in patients without complications is based on expert opinion rather than on data from randomized controlled trials.²

Treat-to-target trial outcomes

Two recent treat-to-target trials have reported clinical outcomes in elderly patients.^{9,10} Both showed no benefit in treating elderly patients to an SBP target of lower than 140 mm Hg compared with SBP targets lower than 150 and 160 mm Hg. A Japanese trial, VALISH (Valsartan in Elderly Isolated Systolic Hypertension Study),⁹ randomly assigned 3079 patients aged 70 to 84 years (mean age 76 years) with isolated systolic hypertension (SBP higher than 160 mm Hg, DBP lower than 90 mm Hg) to a target SBP of lower than 140 mm Hg or 140 to 149 mm Hg. Initial therapy in both groups was 40 to 80 mg of valsartan once a day with other medications, except angiotensin II type 1 blockers, added as necessary to achieve targets. Mean baseline BPs were approximately 170/82 mm Hg in both groups and achieved BPs were 137/75 mm Hg and 142/77 mm Hg in the 140 mm Hg and 140 to 149 mm Hg groups, respectively.

This article has been peer reviewed.
Can Fam Physician 2013;59:19-21

Cet article se trouve aussi en français à la page 22.

After a median of 3.1 years there was no statistically significant difference between the 2 groups in the primary composite outcome of sudden death, fatal or nonfatal stroke, fatal or nonfatal myocardial infarction, death from heart failure, other cardiovascular death, hospitalization for cardiovascular disease, or renal dysfunction (10.6 events per 1000 patient-years vs 12.0 events per 1000 patient-years; hazard ratio 0.89, 95% CI 0.60 to 1.31, $P=.383$).

Published in 2008, JATOS (Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients) studied 4418 Japanese people aged 65 to 85 years (mean age 74 years).¹⁰ Patients had essential hypertension with SBPs of 160 mm Hg or higher while receiving no antihypertensive drugs or receiving the same drug or drugs for at least 4 weeks. They were randomized to an SBP target of less than 140 mm Hg or 140 to 159 mm Hg. The main initial or add-on therapy was a calcium channel blocker, 20 to 60 mg of efonidipine, but other common antihypertensive drugs were also used. Mean baseline BP was 172/89 mm Hg in both groups, and achieved BPs were 136/75 mm Hg versus 146/78 mm Hg in the less than 140 mm Hg and 140 to 159 mm Hg groups, respectively. After 2 years (the pre-specified trial duration), there was no statistically significant difference between the 2 SBP target groups in the primary composite outcome of stroke, cardiac and vascular disease, and renal failure (4.3% vs 4.3%) or withdrawal from adverse events (1.6% vs 1.6%).

The VALISH and JATOS studies have limitations. In both studies, fewer efficacy outcome events occurred than were predicted, with the result that both studies were underpowered. Nevertheless, the results were consistent. In addition, only about 15% of subjects had existing cardiovascular disease, so the studies do not provide information about SBP targets in patients with target organ damage.

No evidence to support treating to target

Another trial, HYVET (Hypertension in the Very Elderly Trial),¹¹ is sometimes used to suggest a SBP treatment target of 150 mm Hg in very elderly patients.² In HYVET, 2 groups of patients, all 80 years of age or older with SBPs at or higher than 160 mm Hg, were assigned a target SBP and DBP of less than 150 mm Hg and less than 80 mm Hg, respectively. However, one group received 1.5 mg of indapamide with or without 2 or 4 mg of perindopril to reach this target, while the other group received a placebo. In the 2 groups, BPs went from a mean of 173/91 mm Hg to 144/78 mm Hg versus 159/84 mm Hg in the treatment and placebo groups, respectively. The study was planned for 5 years but was stopped after a mean of 2.1 years because of a reduction in total mortality (12.3% vs 10.1%, absolute risk reduction 2.2%, relative risk reduction 18%, number

needed to treat 46, 95% CI 24 to 637, $P=.02$). There was no statistically significant difference between the groups in the primary outcome of stroke. While HYVET does provide evidence of benefit from treating hypertension in very elderly patients with indapamide and perindopril, it does not provide evidence to support treating to a specific target.


While VALISH might not have been published in time to influence North American recommendations, current consensus documents and guidelines do not reflect the evidence from drug treatment trials and JATOS, and continue to recommend an SBP target of lower than 140 mm Hg in elderly patients.^{2,7} The ACCF-AHA consensus document does state that for patients aged 80 years or older, achieved SBPs of 140 to 145 mm Hg, if tolerated, can be acceptable with exceptions. For example, if the patient has achieved an SBP lower than 150 mm Hg taking 1 or 2 medications with no problems, it is reasonable to aim for an SBP lower than 140 mm Hg “even though there is no firm evidence to support this target.”² Also, if the DBP is reduced to a “potentially dangerous” level of below 65 mm Hg, the lowest safely achieved SBP of 150 mm Hg or higher is acceptable.² This latter exception indicates potential harm from excessive lowering of BP in very elderly patients.

There is little evidence from randomized controlled trials to guide treatment targets in patients with target organ damage. In many important drug treatment trials in elderly patients, less than 15% of enrolled patients had cardiovascular disease, and patients with serious renal disease were excluded. In JATOS and VALISH, the 2 treat-to-target trials, only approximately 15% of patients had cardiovascular and renal target organ damage.^{9,10} The ACCF-AHA consensus document states there is no evidence to support the use of BP targets lower than 130/80 mm Hg in elderly patients with conditions such as diabetes mellitus, chronic kidney disease, or coronary artery disease.²

Conclusion

Evidence from drug treatment trials indicates there is benefit in treating elderly and very elderly patients with hypertension to an SBP target lower than 160 mm Hg.^{5,8} However, there is uncertainty as to the optimal SBP target implicit in the grade C recommendation of lower than 140 mm Hg regardless of age made by the Canadian Hypertension Education Program.⁷ Drug treatment trials do not provide evidence that lowering SBP to less than 140 mm Hg yields benefits.⁸ In addition, 2 treat-to-target trials provide evidence that lowering SBP to less than 140 mm Hg does not increase benefit compared with SBP targets of lower than 150 or 160 mm Hg.^{9,10} Therefore, the SBP target of lower than 140 mm Hg as recommended by current guidelines is not supported by evidence in elderly patients, a view stated by other

authors.^{2,12,13} Evidence suggests an SBP at or above 140 mm Hg but below 160 mm Hg is acceptable; determining the optimal level will require further study.

The implication for family practice is that physicians might wish to be less aggressive in lowering SBP in elderly patients, particularly if those patients are experiencing adverse effects or cannot afford the multiple drugs required to lower SBP to below 140 mm Hg. 

Dr Allen is Director of Evidence-based Programs in Continuing Medical Education at Dalhousie University in Halifax, NS. **Ms Kelly** is a drug evaluation pharmacist in the Drug Evaluation Unit of the Capital Health Pharmacy Department in Halifax. **Ms Fleming** is Senior Academic Detailer in Continuing Medical Education at Dalhousie University.

Acknowledgment

The Dalhousie Academic Detailing Service is funded by the Nova Scotia Department of Health and Wellness through the Drug Evaluation Alliance of Nova Scotia (DEANS). **Dr Allen** is Director of the Dalhousie Academic Detailing Service and has received funds for research and program development from DEANS. **Ms Kelly** is employed by the Capital Health Drug Evaluation Unit, which receives funding from DEANS. **Ms Fleming** is employed by the Dalhousie Academic Detailing Service. None of the authors receive any form of funding from the pharmaceutical industry.

Competing interests

None declared

Correspondence

Dr Michael Allen, Continuing Medical Education, Dalhousie University, 5849 University Ave, PO Box 15000, Halifax, NS B3H 4R2; telephone 902 494-2173; e-mail michael.allen@dal.ca

The opinions expressed in commentaries are those of the authors. Publication does not imply endorsement by the College of Family Physicians of Canada.

References

1. Chan BT, Schultz SE. *Supply and utilization of general practitioner and family physician services in Ontario. ICES investigative report*. Toronto, ON: Institute for Clinical Evaluative Sciences; 2005. Available from: www.ices.on.ca/file/FP-GP_aug08_FINAL.pdf. Accessed 2012 May 5.
2. Aronow WS, Fleg JL, Pepine CJ, Artinian NT, Bakris G, Brown AS, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *Circulation* 2011;123(21):2434-506. Epub 2011 Apr 25.
3. Stamler J, Stamler R, Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. *Arch Intern Med* 1993;153(5):598-615.
4. Franklin SS. Systolic blood pressure: it's time to take control. *Am J Hypertens* 2004;17(12 Pt 2):49S-54S.
5. Musini VM, Tejjani AM, Bassett K, Wright JM. Pharmacotherapy for hypertension in the elderly. *Cochrane Database Syst Rev* 2009;(4):CD000028.
6. Verdecchia P, Reboldi G, Angeli F, Gattobigio R, Bentivoglio M, Thijs L, et al. Angiotensin-converting enzyme inhibitors and calcium channel blockers for coronary heart disease and stroke prevention. *Hypertension* 2005;46(2):386-92. Epub 2005 Jul 11.
7. Hypertension Canada [website]. 2011 CHEP recommendations for the management of hypertension. Markham, ON: Canadian Hypertension Education Program; 2011. Available from: http://hypertension.ca/images/stories/dls/2011gl/FULLICHEPREcommendations_EN_2011.pdf. Accessed 2012 Dec 4.
8. Mancia G, Laurent S, Agabiti-Rosei E, Ambrosioni E, Burnier M, Caulfield MJ, et al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. *J Hypertens* 2009;27(11):2121-58.
9. Ogiwara T, Saruta T, Rakugi H, Matsuoaka H, Shimamoto K, Shimada K, et al. Target blood pressure for treatment of isolated systolic hypertension in the elderly: Valsartan in Elderly Isolated Systolic Hypertension Study. *Hypertension* 2010;56(2):196-202. Epub 2010 Jun 7.
10. JATOS Study Group. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS). *Hypertens Res* 2008;31(12):2115-27.
11. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrescu D, et al. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008;358(18):1887-98. Epub 2008 Mar 31.
12. Mazza A, Ramazzina E, Cuppini S, Armigliato M, Schiavon L, Rossetti C, et al. Antihypertensive treatment in the elderly and very elderly: always "the lower, the better?" *Int J Hypertens* 2012;2012:590683. Epub 2011 Sep 22.
13. Angeli F, Reboldi G, Verdecchia P. "The lower the BP the better" paradigm in the elderly: vanished by VALISH? *Hypertension* 2010;56(2):182-4. Epub 2010 Jun 7.

— * * * —